

© 2005
JAN 13 2005

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A recombinant influenza virus for expressing high-yield expression of incorporated foreign gene(s), which is genetically stable in the absence of any helper virus and which has eight viral RNA segments, wherein at least one of the regular-endogenous viral RNA segments is replaced by an ambisense RNA molecule (ambisense RNA segment), said ambisense RNA segment containing one of the standard endogenous viral genes in sense orientation and an exogenous a-foreign, recombinant gene in anti-sense orientation, or vice versa, and covalently linked to each other and in overall-convergent arrangement.
2. (Original) The recombinant virus according to claim 1, wherein in the ambisense RNA molecule said foreign recombinant gene is covalently bound to one of the viral genes, while the original vRNA segment coding for the same gene is deleted from the recombinant virus by way of specific ribozyme cleavage.
3. (Previously presented) The recombinant influenza virus according to claim 1, wherein one or more of the regular viral RNA segments, differing from said at least one ambisense RNA segment, comprises a vRNA encoding a foreign gene, preferably one or more of the regular viral RNA segments has (have) been exchanged for a vRNA encoding a foreign gene.
4. (Currently amended) The recombinant influenza virus according to claim 3 in which one or both of the standard glycoproteins hemagglutinin and neuraminidase have been exchanged into-substituted by a foreign glycoprotein(s) or into-by fusion glycoproteins consisting of an anchor segment derived from hemagglutinin and an ectodomain obtained

from the foreign source-glycoprotein, viral or cellular, or in which ~~such said~~ recombinant fusion glycoprotein has been inserted as a third molecular glycoprotein species in addition to the ~~remaining-standard~~ glycoproteins ~~components~~.

5. (Currently amended) The recombinant influenza virus according to claim 1, in which the 5' and/or 3' terminal viral RNA sequences of one or more of the ~~regular endogenous~~ RNA segments and/or of ~~the~~ at least one ambisense RNA segment, ~~which~~ are active as a the promoter signal, and wherein said one or more promoter signals have been modified by nucleotide substitutions in up to five positions, resulting in increased ~~improved~~ transcription rates ~~of both the vRNA promoter as well as the eRNA promoter as present in the complementary sequence.~~

6. (Currently amended) The recombinant influenza virus of claim 5, ~~wherein the~~ wherein one or more RNA segment further comprises a 12 nucleotide conserved influenza 3' terminal sequence that has been modified by replacement of one to three nucleotides occurring in said sequence at positions 3, 5 and 8 relative to the 3' end ~~by other nucleotides~~, and/or ~~wherein the~~ 13 nucleotide conserved influenza 5' terminal sequence that has been modified by replacement of one or two nucleotides occurring at positions 3 and/or 8 in said sequence ~~at positions 3 and 8 by other nucleotides~~.

7. (Original) The recombinant influenza virus of claim 6, wherein the replacements in the 3' terminal nucleotide sequence comprises the modifications G3A and C8U.

8. (Original) The recombinant influenza virus of claim 7, wherein the replacements in the 3' terminal nucleotide sequence comprises the modifications G3A, U5C and C8U, or G3C, U5C and C8G.

9. (Currently amended) The recombinant influenza virus of claim 8, which comprises a 3' terminal nucleotide sequence of 5'-CCUGUUUCUACU-3'. (SEQ ID NO: 26)

10. (Currently Amended) The recombinant influenza virus of claim 6, wherein the 5' terminal nucleotide sequence comprises the modifications U3A and A8U resulting in a 5'-terminal sequence of 5'-AGAAGAAUCAAGG. (SEQ ID NO: 15)

11. (Previously presented) The recombinant influenza virus according to claim 1, which is a recombinant influenza A virus.

12. (Previously presented) The recombinant influenza virus according to claim 1, in which the foreign gene(s) in ambisense covalent junction with viral gene(s) code for proteins and/or glycoproteins which are secreted from cells infected with the recombinant virus.

13. (Currently amended) The recombinant virus according to claim 1, in which the foreign gene(s) in ambisense covalent junction with viral gene(s) code for proteins or artificial polypeptides ~~designed to support an efficient presentation of inherent epitopes capable of being displayed~~ at the surface of infected cells, and wherein said surface display is sufficient to stimulate ~~for stimulation of a B cell and/or T cell response.~~

14. (Currently amended) A method for the production of recombinant influenza viruses as defined in claims 1 comprising

- (a) RNA polymerase I synthesis of recombinant vRNAs in vivo, in ambisense design,
- (b) followed by infection with an influenza carrier strain constructed to include flanking ribozyme target sequences in at least one of its viral RNA segments which is (are) to be replaced by the ambisense segments of step (a), and
- (c) thereafter selective vRNA inactivation through ribozyme cleavage, and wherein active recombinant virus is produced through cycles of virus replication.

15. (Previously presented) A pharmaceutical composition comprising a recombinant influenza virus according to claim 1.

Application No. 09/914,658
Amendment Dated January 18, 2005
Reply to Office Action of January 15, 2004

16. (Currently amended) A method for preventing influenza in a mammal for vaccination purposes which comprising administering an effective amount of a recombinant influenza virus according to claim 1 ~~Method of using a medicament comprising a recombinant influenza virus according to claim 1 for vaccination purposes.~~

17. (Previously presented) The method according to claim 16, wherein the medicament
(a) is suitable against influenza and/or against other infections;
(b) is present in form of inactivated preparations; and/or
(c) is present in form of live recombinant viruses.

18. (Canceled) .

19. (Canceled)

20. (Canceled)

21. (Canceled).

22. (Canceled)

23. (Withdrawn) A method for the production of proteins or glycoproteins which comprises utilizing a recombinant influenza virus according to claim 1 as expression vector.

24. (Canceled)

25. (Original) A method for preventing and/or treating influenza which comprises administering an effective amount of a recombinant influenza virus according to claim 1 to the mammal to be treated.

Application No. 09/914,658
Amendment Dated January 18, 2005
Reply to Office Action of January 15, 2004

26. (Previously presented) A method for somatic gene therapy, which method comprises subjecting the organism to be treated with a recombinant influenza virus according to claim 1.

27. (Withdrawn) A method for transfer and expression of foreign genes into cells, and for transfer and expression of RNA molecules into cells, which method comprises infecting the cells with a recombinant influenza virus according to claim 1.

28. (Canceled)

29. (Canceled)

30. (Canceled)